DETAILED ACTION

Applicant adds new claims 21-23.

Accordingly, claims 1-3, 5-8, 16-18, 21-23 are examined in the instant application.

Claim Rejections - 35 USC § 112, First Paragraph, Enablement

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-3, 5-8, 16-18, 21-23 are rejected under 35 U.S.C. 112, first paragraph, for lack of enablement for a method for detecting cancer, including hepatic cancer, for reasons already of record on paper of 03/11/09.

The response asserts as follows:

The claim is enabled because a person of ordinary skill in the art would be able to measure the GPC3 in the sample, and determine whether a test sample (blood, serum, or plasma) contains "greater levels" of GPC3 than the levels of GPC3 found in a normal control, and thereby be enabled to "identify" a subject/patient suspected of having cancer.

The present invention is not limited to hepatic cancer, but is applicable to the identification of subjects/patient suspected of having other cancers (e.g. lung cancer, colon cancer, mammary cancer, prostate cancer, pancreatic cancer, and lymphomas), as evidenced in paragraph [0007] of U.S. Patent Publication No. 2006/0014223 of the present specification: "The expression of GPC3 protein has also been detected in cancer cell lines other than hepatic cancer

cell lines, such as lung cancer, colon cancer, mammary cancer, prostate cancer, pancreatic cancer, and lymphomas. Hence, GPC3 may possibly be applied to the diagnosis of hepatic cancer as well as many other cancers." Thus, the present invention is not limited solely to hepatic cancer as suggested by the Examiner in the present Office Action.

Applicants reassert that there is no requirement that the skilled artisan use ONLY the claimed method as a final determination before treatment. Applicants respectfully submit that one of ordinary skill can determine whether a test sample (blood, serum, or plasma) contains "greater levels" of GPC3 than the levels of GPC3 found in a normal control, and thereby identify subjects suspected of having cancer, as disclosed in the subject application.

The response has been considered but is not found to be persuasive for the following reasons:

The claimed method cannot distinguish suspected hepatic cancer from liver cirrhosis, because the level of soluble GPC3 in blood or serum or plasma is increased in both hepatic cancer patient and liver cirrhosis as compared to soluble GPC3 in blood or serum or plasma of healthy individual, in view of the teaching of Hippo et al, of record.

Moreover, one cannot predict that the claimed method would be effective in identifying subjects suspected of having cancer, such as lung cancer, colon cancer, mammary cancer, prostate cancer, pancreatic cancer, and lymphomas, because the level of GPC3 in cancer cell lines is not predictably to be the same as that of GPC3 in serum, blood or plasma of patients suspected of having cancer, such as lung cancer, colon cancer, mammary cancer, prostate cancer, pancreatic cancer, and lymphomas, due to the well known cell culture artifacts. Drexler et al, 1993 (Leukemia and Lymphoma, 9:1-25) specifically teach, in the study of Hodgkin and Reed-

Sternberg cancer cells in culture, that the acquisition or loss of certain properties during adaptation to culture systems cannot be excluded and that only a few cell lines containing cells that resemble the *in-vivo* cancer cells have been established and even for the *bona fide* cancer cell lines it is difficult to prove that the immortalized cells originated from a specific cancer cell (see attached abstract). Tian, J et al, 2004 (Physiol Genomics, 17: 170-182), teach culture-induced artifact in macular RPE cells, wherein 950 genes are differentially expressed between native RPE and cultured RPE cells, and wherein 2080 genes are expressed in cultured RPE cells but are not expressed in native RPE cells (abstract, p.176). Similarly, Van Dyke D L et al, 2003 (Cancer Genetics and Cytogenetics 241: 137-141), teach that random loss of chromosome 21 (monosomy 21) in patients with hematologic diseases is rare and should be confirmed by in situ hybridization (FISH), and that in most diagnosed cases the random loss of chromosome 21 is more likely due to artifact of culture of cells obtained from the patients (abstract, and p. 140, first column, last two paragraphs before acknowledgments). Kunkel, P, et al, 2001 (Neuro-oncology 3(2): 82-88), teach that teach that scatter factor/hepatocyte growth factor is overexpressed in most tumors examined, including glioblastomas, and that the lack of expression of scatter factor/hepatocyte growth factor in most cultured glioblastoma cells is not representative of the in vivo situation, and most likely represents a culture artifact (abstract).

New Rejection due to the Amendment

Claim Rejections - 35 USC § 112, First Paragraph, New Matter

Claims 1-3, 5-8, 16-18, 21-23 are rejected under 35 USC 112, first paragraph, as the specification does not contain a written description of the claimed invention.

The limitation of " a method for identifying subjects suspected of having cancer" and "a test sample obtained from a subject suspected of having cancer", claimed in claims 1-3, 5-8, 16-18, 21-23 has no clear support in the specification and the claims as originally filed.

A review of the specification discloses support for a method for detecting cancer by detecting soluble GPC3 in a test or clinical sample (p.1, first paragraph, p.5).

There is nothing in the specification to suggest or disclose " a method for identifying subjects suspected of having cancer" and "a test sample obtained from a subject suspected of having cancer". The subject matter claimed in claims 1-3, 5-8, 16-18, 21-23 broadens the scope of the invention as originally disclosed in the specification.

Conclusion

No claims are allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, THIS ACTION IS MADE FINAL. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however,

will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to MINH-TAM DAVIS whose telephone number is 571-272-0830. The examiner can normally be reached on 9:00 AM-5:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, LARRY HELMS can be reached on 571-272-0832. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

MINH TAM DAVIS
October 22, 2009

/Larry R. Helms/

Supervisory Patent Examiner, Art Unit 1643